Washington University in St. Louis
Office of Technology Management

S1P1-TARGETED PET TRACERS

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Technology Description

Researchers at Washington University in St. Louis have developed sphingosine 1-phosphate receptor 1 (S1P1)-specific PET tracers. Sphingosine 1-phosphate receptors are G-protein coupled receptors, with five subtypes denoted S1P1-5, that have key functions in immune, inflammatory and cardiovascular systems. The expression of S1P1 can be used as a marker for MS, cardiovascular disease and other inflammatory disorders. Therefore, the ability to track S1P1 expression would be beneficial for identifying the disease, monitoring disease progression and assessing therapeutic efficacy. PET imaging is a non-invasive strategy to do this. However, previously developed S1P1-targeted PET tracers had several disadvantages including a requirement for *in vivo* phosphorylation and low specificity for S1P1. Thus, there is still a great need for viable S1P1-targeted PET tracers. To help meet this need and overcome the disadvantages, the inventors have developed these compounds. The compounds have high affinity and selectivity for S1P1, do not require *in vivo* phosphorylation and are not subject to metabolic loss of the radionuclide. This technology provides S1P1-targeted PET tracers that can be used to track S1P1-associated disease progression and monitor therapeutic efficacy.

Stage of Research

PET radioactivity and imaging capabilities have been validated *in vivo* using animal models. Additionally, the e-IND application of 11CS1P1 for human use had been approved by FDA on Dec. 9, 2019.

Related technology

The inventors have also developed sphingosine 1-phosphate receptor 2- specific PET tracers. See Washington University technology T-018580 for more information.

Applications

- PET tracers for S1P1-associated conditions including MS, cardiovascular disease and neuroinflammatory disease
    - Track disease progression
    - Track therapeutic efficacy
- Potential for therapeutic development
- Research tool- investigation into S1P1 role in disease pathogenesis

Key Advantages

- Solves an unmet need- provides a means to track S1P1-associated disease progression and

therapeutic efficacy
- High specificity for S1P1
- Does not require *in vivo* phosphorylation
- Not subject to metabolic loss of radionuclide
- Capable of penetrating the blood brain barrier
- High yield from starting material

Publications

- Rosenberg AJ, Liu H, Jin H, Yue X, Riley S, Brown SJ, Tu Z. Design, Synthesis, and In Vitro and In Vivo Evaluation of an (18)F-Labeled Sphingosine 1-Phosphate Receptor 1 (S1P1) PET Tracer. J Med Chem. 2016 Jul 14;59(13):6201-20. doi: 10.1021/acs.jmedchem.6b00390. Epub 2016 Jun 22.
- Liu H, Jin H, Yue X, Luo Z, Liu C, Rosenberg AJ, Tu Z. PET Imaging Study of S1PR1 Expression in a Rat Model of Multiple Sclerosis. Mol Imaging Biol. 2016 Oct;18(5):724-32. doi: 10.1007/s11307-016-0944-y
- Liu H, Jin H, Yue X, Han J, Baum P, Abendschein DR, Tu Z. PET Study of Sphingosine-1-Phosphate Receptor 1 Expression in Response to Vascular Inflammation in a Rat Model of Carotid Injury. Mol Imaging. 2017 Jan 1;16:1536012116689770. doi: 10.1177/1536012116689770.
- Jin H, Yang H, Liu H, Zhang Y, Zhang X, Rosenberg AJ, Liu Y, Lapi SE, Tu Z. A promising carbon-11-labeled sphingosine-1-phosphate receptor 1-specific PET tracer for imaging vascular injury. J Nucl Cardiol. 2017 Apr;24(2):558-570. doi: 10.1007/s12350-015-0391-1. Epub 2016 Feb 2.
- Luo Z, Rosenberg AJ, Liu H, Han J, Tu Z. Syntheses and in vitro evaluation of new S1PR1 compounds and initial evaluation of a lead F-18 radiotracer in rodents. Eur J Med Chem. 2018 Apr 25;150:796-808. doi: 10.1016/j.ejmech.2018.03.035. Epub 2018 Mar 14.
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- Luo Z, Han J, Liu H, Rosenberg AJ, Chen DL, Gropler RJ, Perlmutter JS, Tu Z. Syntheses and in vitro biological evaluation of S1PR1 ligands and PET studies of four F-18 labeled radiotracers in the brain of nonhuman primates. Org Biomol Chem. 2018 Dec 5;16(47):9171-9184. doi: 10.1039/c8ob02609b.

Patents

- US non-provisional patent application Compositions for binding sphingosine-1-phosphate receptor 1 (s1p1), imaging of s1p1, and methods of use thereof (US2019-0002450-A1)

Related Web Links

- Dr. Tu profile